Myocardial Work

Introduction

This will be an academic exercise. The entire lesson will focus on translating something you already know—the MAP equation—into the myocardial work equation. Conveniently, they are identical. Only instead of using the MAP equation from the perspective of the body, in which the regulators of blood pressure don't care what is altered to improve the MAP (both CO and SVR are affected), we will now assess the equation from the perspective of the heart.

The goal is to show you that the cardiac physiology parameters are all synonyms. We explore each concept mathematically with the MAP equation, graphically with cardiac curves and pressure-volume loops, and metaphorically with a Viking longship analogy. All of them say the same thing, just in different ways. You are reading that correctly. We will say the same thing four times, one of them invoking a Viking longship, to empower you to dominate a subject that has traditionally been extremely complicated.

MAP Equation

In the last lesson, we redefined the MAP equation as the myocardial oxygen demand equation, which was a synonym for myocardial work. We first redefined **preload** as **optimization of sarcomere length** and titin's tension—*more blood in the heart, more blood out*. We then redefined **contractility** as **calcium conductance**, increased by the stimulation of β_1 receptors. Both calcium conductance and sarcomere length are inherent to cardiac myocytes. Together, all myocytes in concert create the **stroke volume**, the volume of blood ejected with each heartbeat. Cardiac output is stroke volume times heart rate. In this lesson, we limit our focus to a single contraction, so heart rate can be ignored. From the body's perspective, if tissues are perfused, the body is happy. Said differently, if the MAP is normal, the body is perfused. Now we are changing perspective from that of *the body's perfusion* to *work the heart must do.* All elements of the MAP equation (CO, HR, SV, CONT, PL, SVR) have the same mathematical relationship to myocardial work—increase any, and the heart must work harder.

But there is a key change. **SVR opposes cardiac output**. The heart contracts to eject blood. If the resistance to the blood being ejected into the aorta is increased, the heart must either generate more force to overcome it or eject less blood. To open the aortic valve and eject blood, the pressure in the ventricle must be higher than the systemic vascular resistance pushing back on it. **The higher the SVR, the more work the heart must do to overcome it.**

The complexity of this lesson is in the introduction of new parameters—volumes. The **end-systolic volume (ESV)** is the volume of blood in the heart at the beginning of diastole—how much is left over after ventricular ejection ends. The **end-diastolic volume** (EDV) is the volume of blood in the heart at the beginning of systole. The **EDV is a synonym for preload**. *More blood in the heart, more blood out of the heart*. The higher the EDV, the more volume there is, the higher the preload, the more optimization of sarcomere length and passive titin tension, the harder the ventricle will contract. The difference between the two is the **stroke volume** (SV), which now has a mathematical representation. Increased EDV, increased SV, increased CO, increased work.

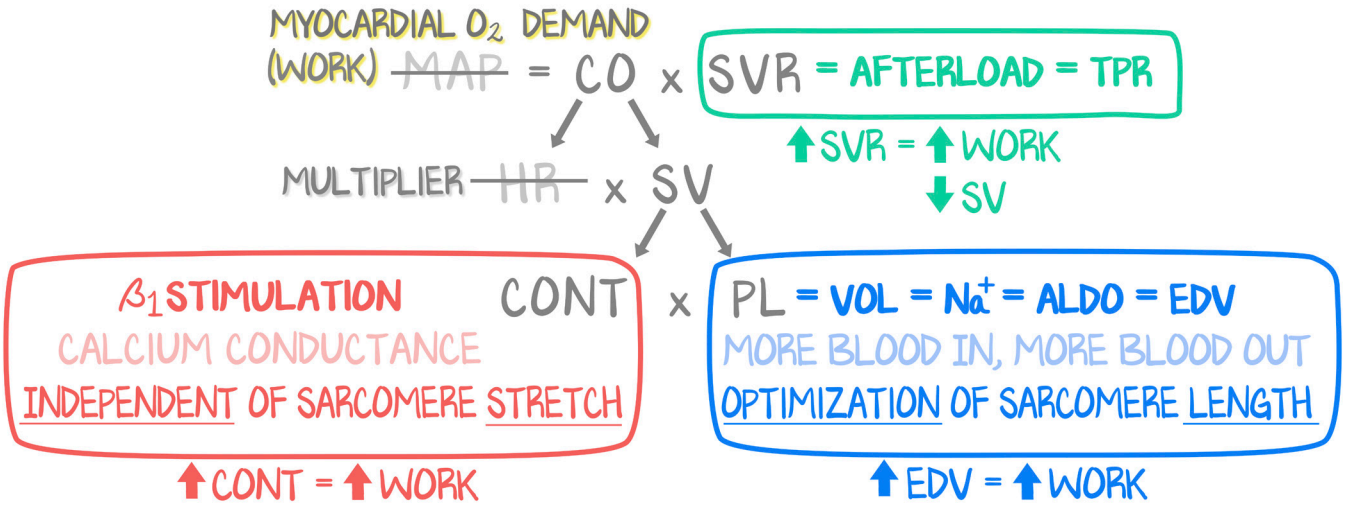

Figure 5.1: The MAP Equation
Mean arterial pressure is a product of cardiac output and systemic vascular resistance. The cardiac output is a product of stroke volume (the amount of blood that comes out of the ventricle with each beat) and heart rate (the number of times per minute it ejects that stroke volume). Stroke volume is dependent on how much volume is in the ventricle (preload) and how powerful the ventricle is primed to be (contractility). You are not supposed to have comprehension the first time you see this. By the end, you will.

The OnlineMedEd Viking Ship

Because this lesson says the same thing in multiple ways—MAP equation, cardiac output/input curves, and pressure-volume loops—we wanted to introduce our own rendition. The goal is to completely dissociate the cardiac physiology parameters from the concept being taught. Many learners get caught up in the technical jargon. Dr. Williams uses the MAP equation (his own Dustynism), and we asked our illustrator to find a way to depict the concepts as she understood them. Dr. Williams uses the weightlifting analogy in the video, but that doesn't work for all parameters. Our illustrator was able to solve the problem using a representation completely unrelated to medicine that encompasses all three parameters. If you know boats/sailing/the sea, please go along with the analogy for the sake of everyone else who doesn't. The analogy works, but we had to make some simplifications. Follow along with Figure 5.2.

The analogy is a Viking longship, a ship with sails AND oars. To move on the ocean, the ship's crew can either use the wind in the sails (which the crew maintains) or use the oars to row. Either way, the ship moves, and the crew expends energy—work. Most of the crew is idle and does not expend any energy but can be called upon when needed. More crew active, more energy spent, and both wind in the sails or oars in the water require more crew. This clicks with different learners in different ways. If considering only stroke volume—and not cardiac output, which requires incorporating heart rate—distance works better. All the crew stroke (pull the oars) at the same time. It's easy to see how more rowers require more energy. The distance the ship travels with one stroke is both limited by the current (in our model, the current is always against us) and aided by the wind in the sails (likewise, the wind is always in our sails). If considering cardiac output—which incorporates heart rate, beats per minute—speed works better. The ship travels a distance with each stroke (heartbeat) and travels faster with more rowers. The wind in the sails propels the ship forward faster, and the current opposes the ship, slowing it down.

The wind in the sails represents **preload**. The more wind there is, the farther/faster the ship will move. But because it takes more crew to manage the sails in strong winds, more wind in the sails means more effort by the crew (work). The number of rowers represents **contractility**, the degree of calcium

conductance. The more rowers there are, the farther/faster the ship will go. More crew rowing to move the ship faster obviously expends more energy than fewer crew rowing. Together, the preload and contractility contribute to stroke volume and myocardial work. Together, the wind in the sails and the oars in the water contribute to the ship's distance/speed and energy expended by the crew.

The ship travels on the surface of the ocean, and the current is always against the ship's direction of travel. The current represents **afterload**. The stronger the current, the slower the ship moves/the less distance it covers. Alternatively, the crew can put more oars in the water—work harder—to move just as far/fast as against a weaker current. The current opposes the wind in the sails and the oars in the water. Afterload opposes stroke volume and cardiac output. A strong current makes the crew work harder to go just as far/fast. Afterload increases myocardial oxygen demand, increases myocardial work.

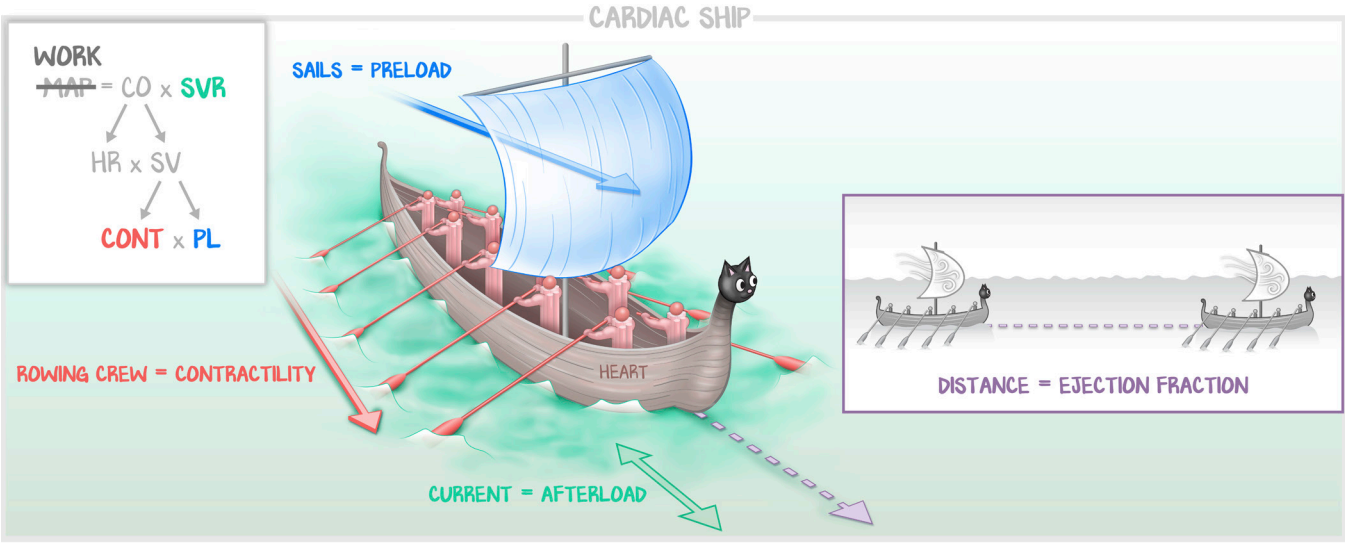

Figure 5.2: Myocardial Oxygen Demand via the OME Viking Longship

The distance the ship moves represents the **stroke volume** (ejection fraction, force of contraction). This one is the biggest stretch, but just go with the analogy—the wind and rowing together propel the ship forward against the current. If the crew adds rowers and changes nothing else, does the ship move faster or slower? More rowers move the ship faster and farther. Is the crew spending more energy or less? More rowers means more energy spent. Both the work done by the crew (myocardial oxygen demand) and the distance/speed traveled (stroke volume) increase. More wind in the sails means more crew are required to maintain the sails. More wind means faster/farther travel (stroke volume) and more energy from the crew (myocardial oxygen demand). A strong countercurrent makes it harder to go as far and as fast as if there were calm waters and no current opposing the ship and crew. The crew must work harder (myocardial oxygen demand) to overcome a strong current (afterload), so they expend more energy to go just as far/fast.

Of course, this does require some suspension of disbelief—the current is always unfavorable, and the wind is always favorable—but it is our attempt to offer a less technical means of learning the information, enabling you to then translate it into curves and loops. We will explain the coming topics using the MAP equation, the curves and loops, and the Viking ship. Only one method needs to work.

And one final note—**the longship analogy works for myocardial oxygen demand and stroke volume, but not for the MAP**.

Preload Is Venous Return

Preload is a volume. Preload is the volume of blood that fills a ventricle during diastole. At the end of diastole, the maximum amount of blood in the ventricle just as the mitral valve closes and systole begins is the **end-diastolic volume** (EDV). The EDV is a volume. Volume takes up space. The ventricle squeezes blood out of the chamber during systole. To do that, sarcomeres shorten. Myocytes shorten. The ventricle contracts from the bottom of the ventricle up toward the aortic valve. The ventricle shortens.

The ventricle relaxes in diastole. It fills with volume. The ventricle lengthens because the myocytes lengthen because the sarcomeres lengthen. At physiological values, the filling of the ventricle with blood will always serve to improve the actin-myosin overlap. Remember, this is an academic lesson. More volume will stretch the cardiac myocytes, optimize their sarcomere length, and increase calcium-dependent calcium release. However, we are being rigid to the method. Preload is the EDV, and the EDV increases stroke volume, cardiac output, and work because of the optimization of sarcomere length and passive titin tension.

The more blood put into the ventricle during diastole, the more blood comes out during systole.

Preload improves the efficiency of the ventricular contraction. More preload increases the MAP. Said practically, giving a 2-liter bolus of saline to a patient in septic shock improves the blood pressure. Losing 2 liters of blood from a gunshot wound critically compromises blood pressure.

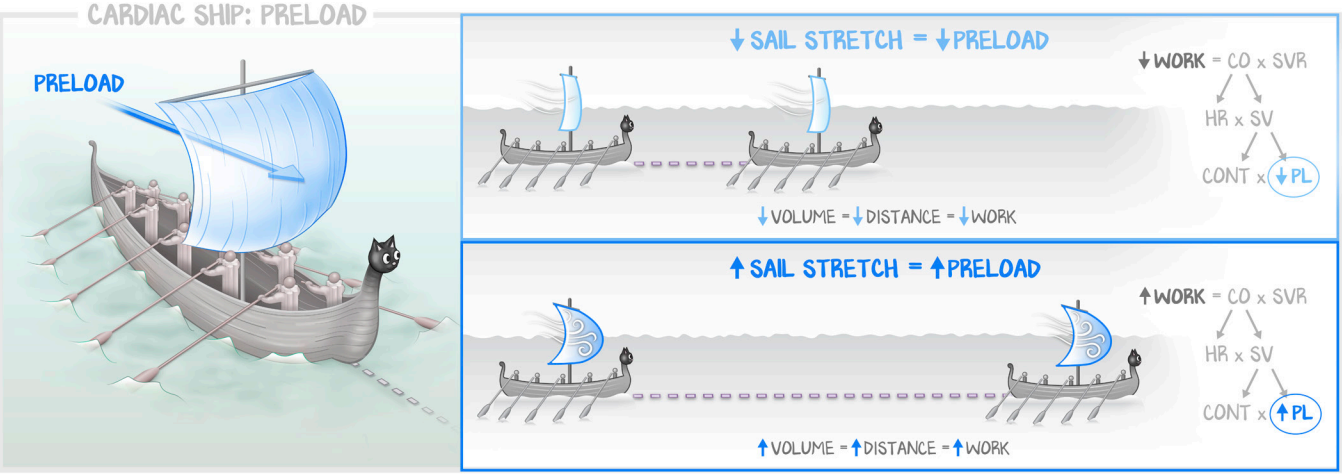

Figure 5.3: Preload
If the number of oars in the water doesn't change, and the current doesn't change, and the amount of wind in the sails increases, the ship will move farther/faster than with less wind. Because more wind requires more crew to maintain the sails, the amount of energy spent to go farther/faster increases. Said technically, with an increase in volume during diastole (increased EDV), the stroke volume will increase at the expense of increased myocardial oxygen demand.

A greater force of contraction means more ATP is used, which means the amount of work increases; thus, an **increased force of contraction increases myocardial oxygen demand**. If the heart works harder (English language "work"), the cardiac work (Physiology "work") increases, and therefore the need for oxygen increases.

Contractility Is Calcium Conductance

Contractility is the baseline strength of the ventricle. Contractility is how pumped up the ventricle is regardless of the volume given. This is not ventricular hypertrophy, atrophy, or density. Contractility in the MAP equation is how hard the ventricle can beat and is independent of preload. But the last section

just explained how preload increases the ventricular force of contraction. Contractility in the MAP equation needs to be associated with an independent intracellular phenomenon other than stretching myocytes. Because myocytes use calcium to contract, and more calcium means more forceful contraction, think of contractility as the **baseline myocyte conductance to calcium**.

If a myocyte has more L-type voltage-gated Ca^{2+} channels ready to open, more L-type channels will open when a depolarization arrives on that myocyte. The Ca^{2+} membrane conductance goes higher. More calcium-induced calcium release happens because more calcium opens more RyR2 channels. More calcium rushes into the cytoplasm from the sarcoplasmic reticulum. More calcium, more force of contraction. If that same myocyte has fewer L-type voltage-gated Ca^{2+} channels ready to open, then when that depolarization comes, the initial L-type influx will be smaller, the RyR2 response smaller, and the force of contractility weaker.

The state of ion channels on the sarcolemma, on the cell membrane, determines the baseline calcium conductance. Ion channel state is manipulated by the autonomic nervous system. The ventricles are innervated by the sympathetic nervous system and not the parasympathetics. Norepinephrine activates β_1 receptors on ventricular myocytes. Through the G_s-AC-cAMP pathway, the downstream effect is an increased membrane conductance to calcium.

More sympathetic stimulation, more cAMP, higher membrane conductance to calcium, more calcium on depolarization, stronger force of contraction. Less sympathetic stimulation does the opposite. Parasympathetic tone does not influence the ventricular force of contraction. More contractility means more calcium, more ATP, more work, and **higher myocardial oxygen demand**.

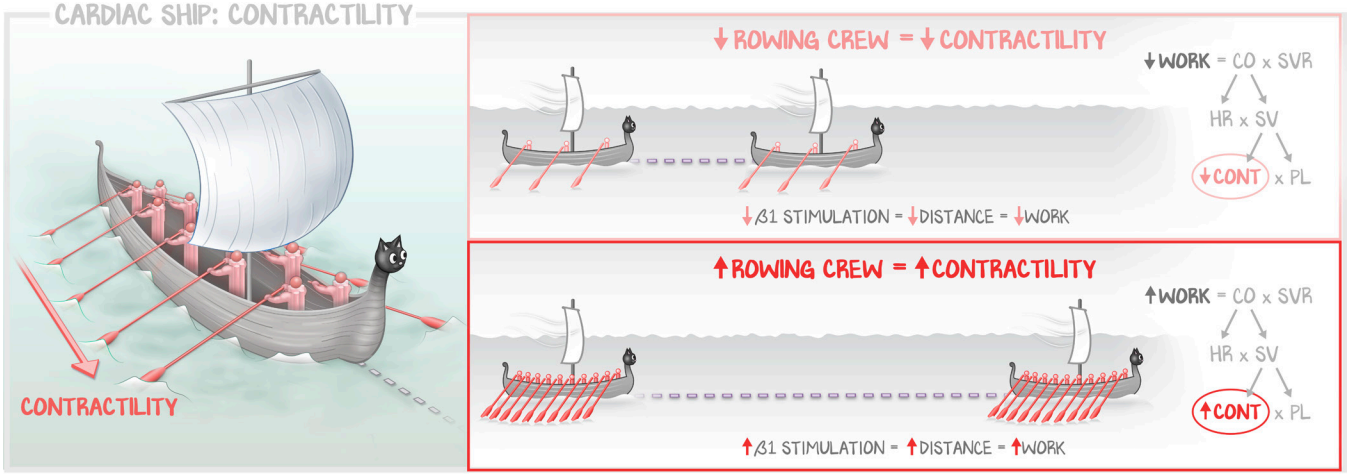

Figure 5.4: Contractility
If the wind in the sails doesn't change, and the current doesn't change, and the number of oars in the water increases, the farther/faster the ship will move. More crew dedicated to rowing means the energy spent by the crew increases. Said technically, an increase in calcium conductance (contractility) increases stroke volume at the expense of increased work. Decreasing contractility will decrease the stroke volume and decrease the work of the heart.

Systemic Vascular Resistance Is Afterload

Blood pressure is supported by systemic vascular resistance. When the systemic vascular resistance is clamped down, the resistance through the system is higher. A higher resistance in a circuit means the pressure is higher to achieve the same flow. Consider what happens when you lose a liter of blood from a gunshot wound. The tank—your vasculature—had been filled, the blood pressure good before that blood loss. Now one-fifth of the tank is empty. By vasoconstricting, the tank can be made smaller. Now four liters fills what used to be a 5-liter tank. The MAP is maintained.

But what does that do to the heart? A higher resistance means a higher pressure. A higher pressure in the aorta. A higher pressure pushing back on the aortic valve, keeping it closed. A higher pressure the ventricle must fight against to open the aortic valve. A higher pressure to overcome to eject blood during systole.

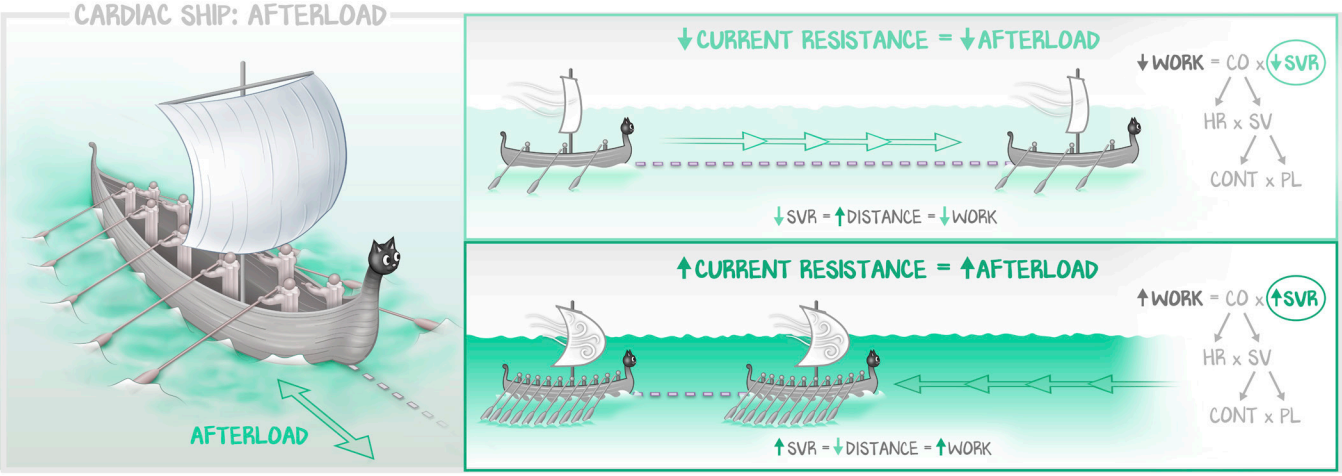

Figure 5.5: Afterload
If the number of oars in the water doesn't change, and the wind in the sails doesn't change, and the countercurrent increases, the ship doesn't move as far/fast. But the crew has a choice: same crew/effort but don't move as far, or dedicate more crew/effort to moving farther/faster. Said technically, an increase in afterload reduces the stroke volume if the heart doesn't work harder. Either the heart increases stroke volume (by increasing contractility), incurring a higher oxygen demand, or the stroke volume is compromised. Because the body won't allow the MAP to be compromised, it tells the heart to work harder, shouting at the crew members to row harder and faster to maintain distance/speed at the cost of even more cardiac work, with higher myocardial oxygen demand. We'll capitalize on this in the next lesson.

A higher systemic vascular resistance means the heart must work harder to expel the same volume of blood, thereby **increasing the myocardial oxygen demand**. Systemic vascular resistance, afterload, total peripheral resistance, α_1 stimulation, AT_2 stimulation, and arterial tone are all synonyms. If they go up, the work goes up, which is the same as saying the myocardial oxygen demand goes up.

Heart Rate Affects Myocardial Work

Let's keep the discussion simple and restricted to the equation. If all other parameters of the MAP equation are held constant, increasing the heart rate will increase the MAP and increase the myocardial oxygen demand. Conversely, if all other parameters are held constant, decreasing the heart rate will decrease the MAP and decrease the myocardial oxygen demand.

In the longship, the speed at which the crew members row is the heart rate. Think about that for a moment. Rowing takes time. The oars have to come out of the water, be positioned, placed in the water, and then pulled. If the crew members row too fast, they either spend less time with the oars in the water or they won't row as hard, all the while still expending a lot of energy to do it. There are diminishing returns to heart rate. If the heart rate goes too fast, the ventricle cannot fill. Without filling, without preload, the stroke volume will decrease, cardiac output will be compromised, and the MAP will fall, all the while the myocardial oxygen demand increases.

Conversely, if the crew members row too slowly, or worse, not at all, the crew will be well rested but won't move very fast. Slow heart rates allow for the ventricle to fill, each heartbeat providing a high stroke volume, but compromise cardiac output, compromising the MAP with reduced myocardial oxygen demand.

Cardiac Output Curve

What we did with math using the ~~MAP~~ myocardial work equation, we are going to reiterate using graphs and pressure-volume loops. Different researchers conducted different studies, and each measured something different. Because all those researchers did a lot of research a long time ago, we now have the privilege of using shortcuts and Viking longships to explain it. The revelation we had in preparing this material for you is that although there are only two parameters to the cardiac output and cardiac input curves, those two parameters have many names. On the following graphs, the x-axis is EDV. EDV, aldosterone, sodium, preload, volume, and wind in the sails can be used on the x-axis interchangeably. The y-axis is labeled force of contraction. Force of contraction (OME's term and a Dustynism), cardiac output, stroke volume, venous return, myocardial work, myocardial oxygen demand, and distance/speed the longship travels can be used on the y-axis interchangeably.

Doctors Frank and Starling came up with some great data. Their data said that *the more blood in the heart, the more blood out of the heart*—increasing volume/preload increases cardiac output. The **Frank-Starling** curve, also known as the **cardiac function** curve and the **cardiac output** curve, gives us a visual representation of the MAP equation's blue box, of the wind in the sails. For every **increase in preload** (to the right on the x-axis), the **force of contraction will increase** (up on the y-axis). Look at Figure 5.6a only. Then come back here. The **shape of the Frank-Starling curve** is the blue box in the MAP equation; it is the force of contraction caused by the optimization of sarcomere length and titin's passive tension.

Now a thought exercise. If you keep the volume constant and change only the contractility, what will happen to the force of contraction? Mathematically, because stroke volume is preload times contractility, if contractility increases, the stroke volume increases. Said more accurately, with increased contractility, for a given volume/preload (y-axis), there will be a more forceful contraction (x-axis) as compared to with lower contractility. Graphically, **higher contractility shifts the curve up and to the left**. Conversely, decreasing contractility shifts the curve down and to the right.

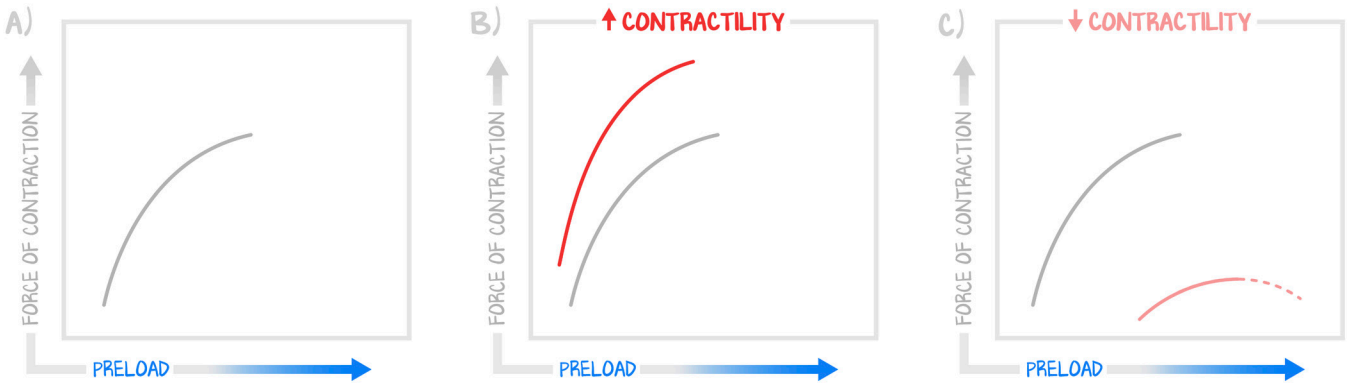

Figure 5.6: Cardiac Output Curve and Contractility
(a) The force of contraction is mapped as a function of preload. As preload increases, the force of contraction increases.
(b) With increased contractility, the force of contraction is higher than with baseline contractility for every preload value.
(c) With decreased contractility, the force of contraction is lower than with baseline contractility for every preload value.

Now a second thought exercise. This one is harder because it isn't clearly represented in the MAP equation. What happens to the cardiac output curve when systemic vascular resistance changes? First, what does it do to the myocardial work? SVR goes up, work goes up. Mathematically, if SVR goes up and cardiac output doesn't change, work goes up. Said differently, the heart must use more energy to maintain the ejection of blood (the stroke volume) and overcome the increased SVR. **OR** the work stays constant, and the cardiac output falls. Cardiac output falls because the stroke volume falls. The SVR

opposes cardiac function, resists the ejection of blood. So, for every volume (x-axis), less blood comes out than if SVR were not increased. **Increasing SVR shifts the cardiac output curve down.** And the inverse is true: decreasing SVR shifts the cardiac output curve up.

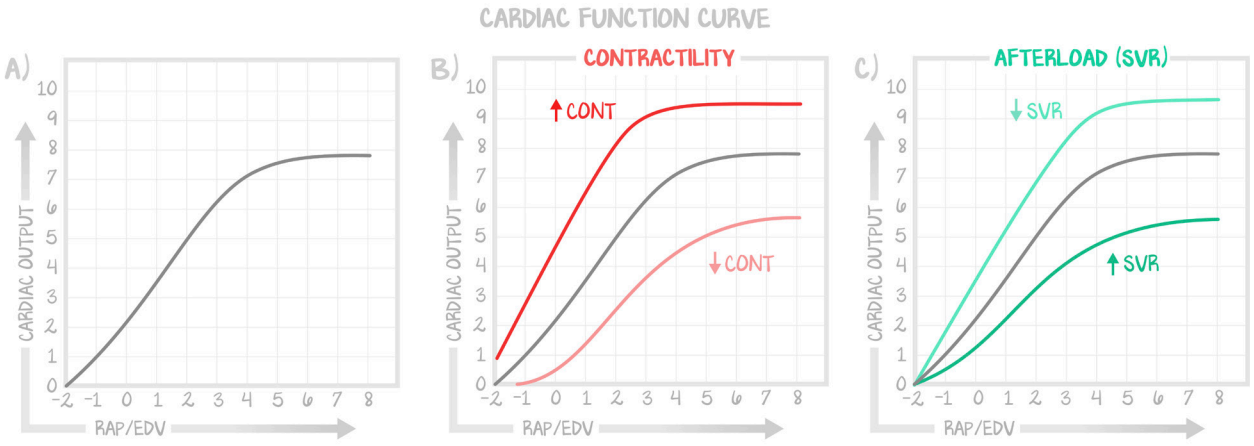

Figure 5.7: Cardiac Function Curve
(a) Normal Curve, as EDV/RAP goes up, cardiac output goes up. (b) Changes in contractility shift the slope of the curve. (c) Afterload shifts the curve up and down. Cardiac function, cardiac output, force of contraction, and Frank-Starling all say the same thing, even though they don't look identical.

Cardiac Input Curves

If there is a cardiac output curve, then there must be a cardiac input curve. Cardiac input (OME's term) is known as the vascular function curve and the venous return curve. It has a shape. Do not attempt to understand it. Increases in **systemic vascular resistance change the slope of the curve** (y-axis intercept changes, x-axis intercept does not), whereas changes in **volume move it up and down**. Look at the shape of the curve in Figure 5.8. There are a y-axis and an x-axis, which are labeled the same as the x-axis and y-axis labels of the cardiac output curve. See how the x-intercept and the y-intercept change with preload and how systemic vascular resistance does not alter the x-intercept but does alter the y-intercept.

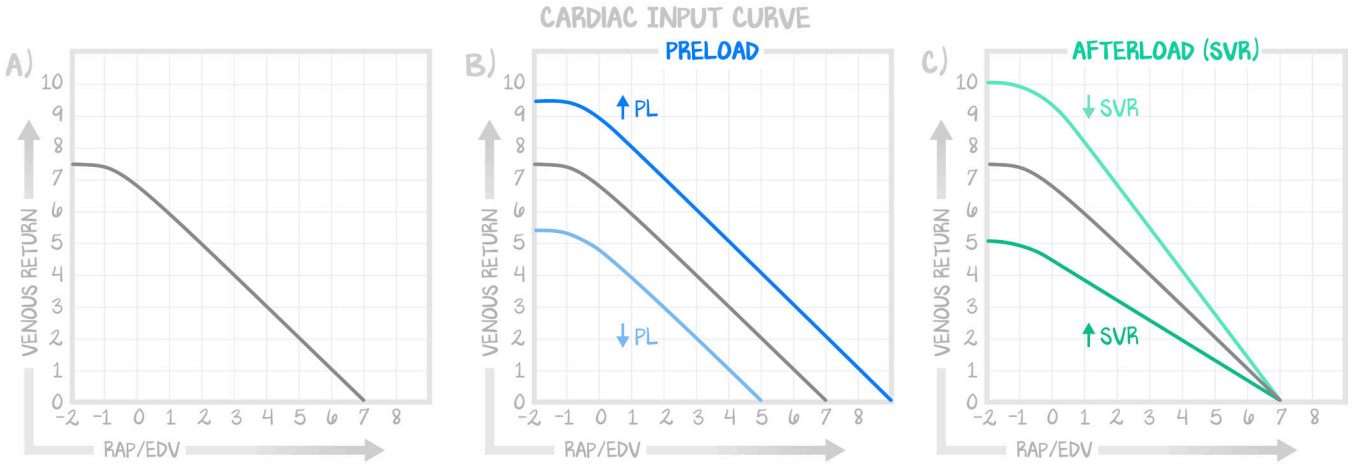

Figure 5.8: Cardiac Input Curves
(a) Normal cardiac input curve. (b) Volume, preload, shifts the curve up and down, changing both the x- and y-intercepts. (c) Afterload does not change the x-axis but does change the y-axis. Increased SVR shifts the curve down, just like it did to the cardiac output curve. Don't think too hard about this, just get the question right on your licensing exam.

Putting Them Together

Get ready for it; this is what all these curves have been about: TEST PREP!

The cardiac output curve shifts up and to the left with increased contractility, shifts down with increased systemic vascular resistance, and is not affected by preload. **Infer the inverse.**

The cardiac input curve shifts up and to the right (the x-intercept and y-intercept are greater) with increased blood volume, shifts down with increased systemic vascular resistance, and is not affected by contractility (as calcium conductance). **Infer the inverse.**

If you plot both on the same graph, they **intersect**. That intersection is called the equilibrium pressure. The test will then inform you that something has changed—SVR, CONT, or PL will go up or down—and you will need to determine what will happen to the equilibrium pressure. Or, the test will demonstrate a change in the intercept, and you will have to determine which parameter changed. Keep in mind, **in life, one cannot alter one parameter without affecting the other, so this exercise is purely academic**.

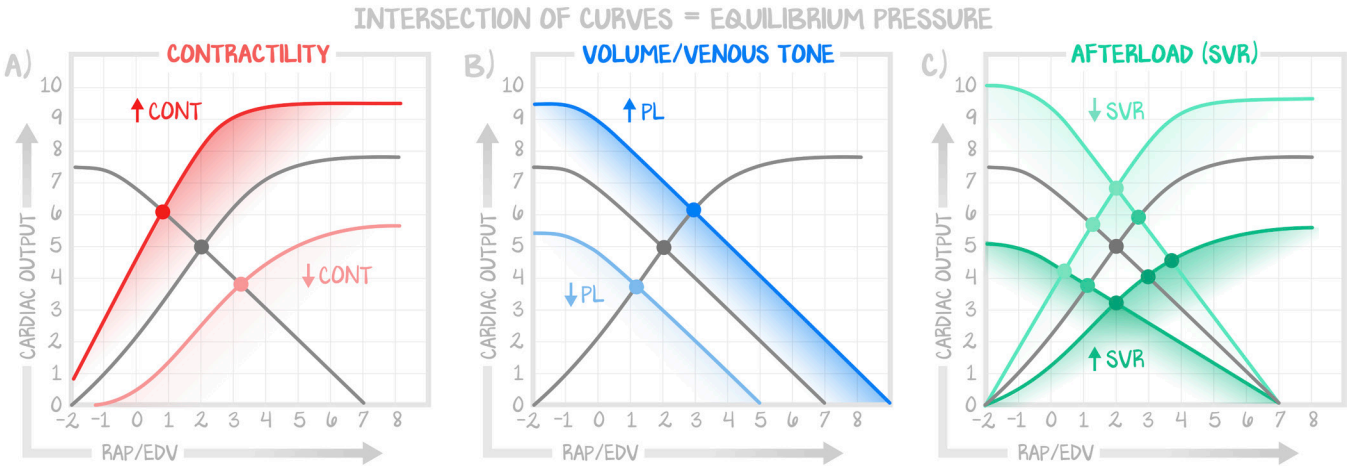

Figure 5.9: Intersection of the Cardiac Curves

Let's Start Talking Pressure-Volume Loops

Pressure-volume loops are another way of representing myocardial work, stroke volume, and SVR, PL, and CONT. The details of the cardiac cycle are in the Plumbing island. You don't need the details to follow along. A pressure-volume loop displays volume on the x-axis and pressure on the y-axis. The pressure is the pressure within the ventricle. Pressure-volume loops are so commonly used on licensing exams because they visually represent the ~~MAP~~ myocardial oxygen demand equation.

Pressure-volume loops communicate **myocardial work** as the **area under the curve**. Pressure-volume loops communicate **stroke volume** by the difference between the EDV and the ESV (the horizontal boundaries of the curve, the distance along the x-axis). Pressure-volume loops can alter one of three parameters that conveniently align with the MAP equation—ESPVR (contractility), EDV (preload), and the opening pressure (SVR). Pressure-volume loops **do not communicate time**. One loop is one cardiac cycle.

Let's briefly preview the cardiac cycle from the perspective of the left ventricle. Depolarization of the muscle. Systole begins. The ventricle contracts; sarcomeres begin to shorten. The mitral valve closes. When it does, it makes a sound. The pressure in the ventricle is greater than in the atrium —that's why the mitral valve closed closed—but not greater than the systemic vascular resistance. The pressure in the ventricle

increases until it exceeds the opening pressure of the aortic valve, which is systemic vascular resistance. The aortic valve opens, sarcomeres shorten, and blood is ejected. Sarcomeres reach their maximally contracted state (as small as they are going to get), and the ventricle relaxes. When the pressure in the ventricle goes below the systemic vascular resistance, the aortic valve closes and makes a sound. The mitral valve is still closed, so the ventricle continues to relax but doesn't change its volume. When the pressure in the ventricle drops below the pressure of the atrium, the mitral valve opens, and the ventricle begins to fill. When the mitral valve closes, the phase is called isovolumetric contraction—pressure (y-axis) goes up, volume (x-axis) doesn't change. When the aortic valve closes, the phase is called isovolumetric relaxation—pressure (y-axis) goes down, volume (x-axis) doesn't change. During diastolic filling, the ventricle increases in volume (x-axis increases, y-axis stays the same). During systolic ejection, the ventricle decreases in volume, and some stuff happens that makes it more complicated and gives it a domed shape.

The volume of blood in the ventricle right before the mitral valve closes is the largest volume of blood in the heart for that beat. It is the volume at the end of diastole, the **end-diastolic volume**. EDV is **preload**. The volume of blood in the ventricle right before the aortic valve closes is the smallest volume of blood in the heart for that beat. It is the volume at the end of systole, the **end-systolic volume**. The **stroke volume** in the MAP equation is a combination of preload and contractility. The **stroke volume**, the medical term outside the MAP equation, is defined by how much blood is expelled from the ventricle in one beat. It is mathematically defined as the EDV minus the ESV. The **ejection fraction** is the percent of the EDV that came out during the beat (SV ÷ EDV).

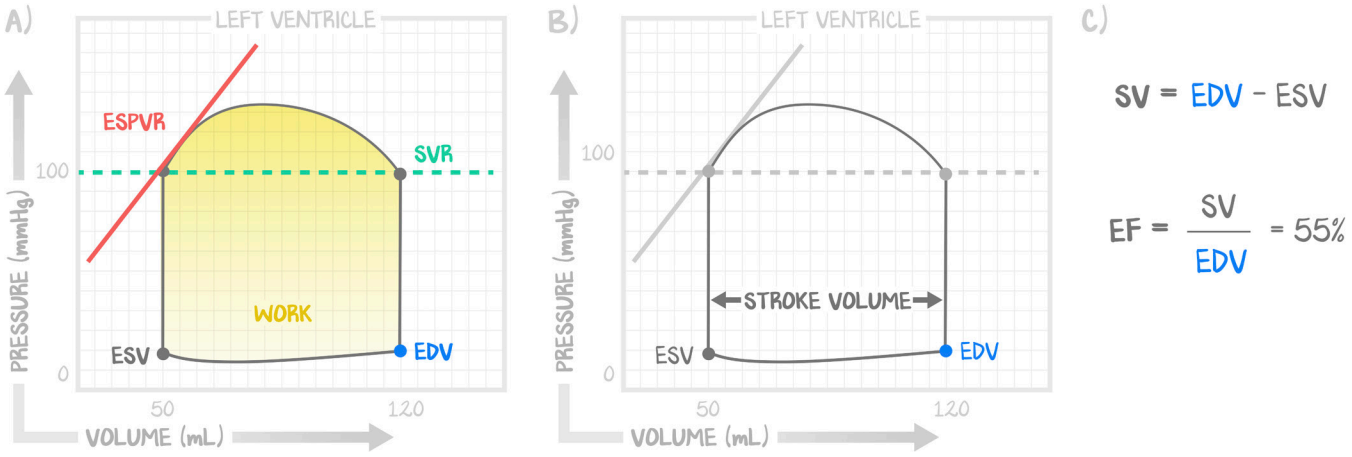

Figure 5.10: Stroke Volume
(a) The area under the curve, enclosed by the pressure-volume loop, is the total work done. The higher the EDV (preload), SVR (afterload), or ESPVR (contractility), the more work. These are now representations of the ~~MAP~~ work equation pictorially. (b) Stroke volume represented visually on an intact ventricular pressure-volume loop. The stroke volume is the amount of blood that comes out off the ventricle during systole. That volume is the distance between end systolic volume and end diastolic volume. (c) Stroke volume and ejection fraction represented mathematically. Normal is around 55%.

The **opening pressure** is **afterload**. A higher afterload will cause the aortic valve to open later, at higher ventricular pressures, and it will close the aortic valve sooner. Less blood comes out and at higher ventricular pressures. A higher afterload will get less blood out, thereby decreasing stroke volume and subsequently increasing ESV and increasing work. Infer the inverse.

The **ESPVR** is **contractility**. The ESPVR will shift up and to the left with increased contractility (like the cardiac output curve) and will shift down and to the right with decreased contractility. Higher contractility results in more blood out of the heart, and therefore a decreased ESV, larger stroke volume, and increased work. Infer the inverse.

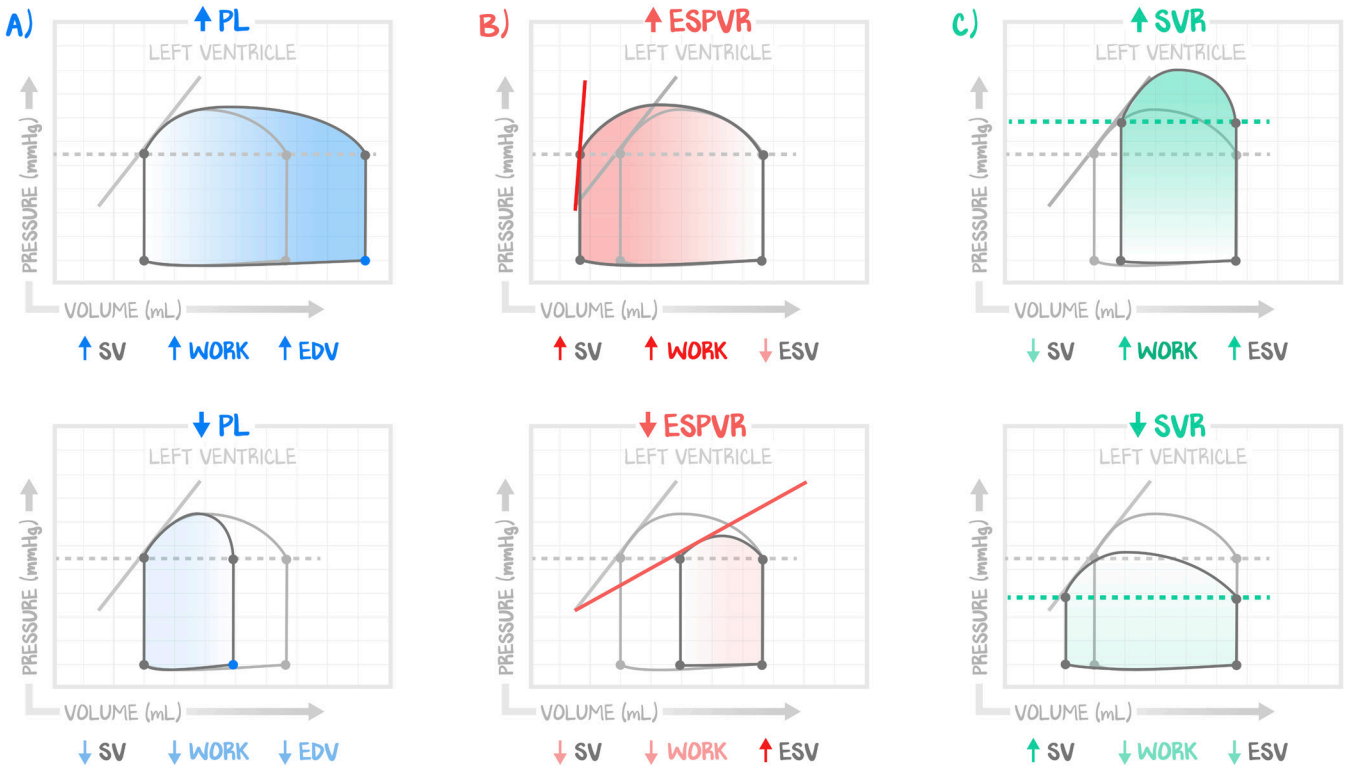

Figure 5.11: Simplified
(a) Shows a shift in preload. Preload changes the EDV. Increasing preload increases stroke volume. Decreasing preload decreases stroke volume. (b) Shows changes in contractility. Increases in contractility improve stroke volume. If stroke volume goes up and preload (EDV) stays the same, that means the ESV must be lower (shifted to the left). Decreases in contractility do the opposite. (c) Afterload changes the volume at which the aortic valve closes. It prevents the blood from coming out, reducing stroke volume. Since preload (EDV) doesn't change, that means the ESV must move. Increased afterload shifts the ESV right.

The Ejection Fraction

The clinically useful measurement for cardiac function is the ejection fraction. The fraction (percentage) of the blood in the ventricle at the beginning of systole compared to the blood that gets ejected. A normal ejection fraction is 55%. When an echocardiogram is performed, the ejection fraction can be measured by the cardiology technician or eyeballed by a trained cardiologist. A reduced ejection fraction implies a weak heart (systolic heart failure) and impaired contractility. An increased ejection fraction implies a hyperdynamic system—the heart is compensating for some other insult elsewhere, beating stronger in response to sympathetic stimulation. Look for volume loss and causes of vasodilation (such as sepsis).

In physiology, the ejection fraction is an equation that harnesses the ESV and EDV shifts from the last section—in theory only. The MAP equation is what happens in people. Keeping all variables constant and altering only one on exams is theory only and does not happen in people. Here's the physiology discussion for you.

$$EF = SV/EDV \qquad EF = \frac{EDV - ESV}{EDV}$$

EDV is shifted by preload. ESV is shifted by afterload (SVR) and contractility. If you don't change the preload (EDV constant), then a bigger ESV means a smaller EF. Bigger ESV from the last section was caused by increased afterload (as in hypertension) or decreased contractility (as in heart failure).